Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1.-14. (Canceled)

15. (Currently Amended) A method for identifying ~~an~~ a candidate agent that interacts with P-selectin LE, comprising the steps of:

(a) utilizing the x-ray structural coordinates of P-selectin LE according to Figure 2, Figure 3, or Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, to generate a three-dimensional model;

(b) identifying the amino acid residues forming the active site of said P-selectin LE from the three-dimensional model in step (a) in order to generate a three-dimensional representation of the active site of P-selectin LE.

~~providing a crystal comprising a P-selectin LE, wherein the crystal has a space group $P2_1$ or I222 and the P-selectin LE comprises an the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:9, or conservative substitutions thereof;~~

~~obtaining the relative structural coordinates of an active site of said P-selectin LE crystal,~~ wherein the ~~relative~~ x-ray structural coordinates of the active site of said P-selectin LE are selected from the group consisting of:

(i) the ~~relative~~ x-ray structural coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å;

(ii) the ~~relative~~ x-ray structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, LYS111, and LYS113 according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

(iii) the ~~relative~~ x-ray structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYS113, and HIS114 according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å;

(c) employing said three-dimensional representation from step (b) to identify said candidate agent that interacts with the active site of P-selectin LE;

(d) synthesizing said candidate agent;

(e) contacting said candidate agent with said P-selectin LE to determine the ability of said candidate agent to interact or bind with said P-selectin LE;

whereby the detection of the ability of said candidate agent to interact or bind said P-selectin LE, thereby identifies said candidate agent as a agent that interacts with P-selectin LE.

~~generating a three dimensional model of P-selectin LE using said relative structural coordinates of the active site of the P-selectin LE crystal evaluating the fit between the three-dimensional model of the active site and a candidate agent thereby identifying the agent.~~

16. (Currently Amended) The method of Claim 15, further comprising the step ~~steps~~ of:

~~obtaining the identified agent; and~~

contacting the ~~identified~~ candidate agent with P-selectin LE in order to determine the effect the agent has on P-selectin LE activity.

17.-35. (Canceled)

36. (Currently Amended) The method of claim 53 [[15]], wherein the step of determining ~~evaluating~~ the fit between the three-dimensional representation ~~three dimensional model~~ of the active site of P-selectin LE and the three-dimensional structure of the candidate agent comprises

performing computer fitting analysis of the candidate agent with the three dimensional representation. ~~model.~~

37. (Canceled)

38. (Currently Amended) The method of claim 15, wherein the candidate agent is selected or designed to interact with the active site of P-selectin LE.

39. (Currently Amended) The method of claim 15, wherein the ~~relative~~ x-ray structural coordinates of the active site of P-selectin LE comprise the ~~relative~~ structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, LYS111, and LYS113 ~~the active site of P selectin LB crystal~~ according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

40. (Currently Amended) The method of claim 15, wherein the ~~relative~~ x-ray structural coordinates of the active site of P-selectin LE comprise the ~~relative~~ structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYS113, and HIS114 ~~the active site of P selectin LE crystal~~ according to Figure 5 ~~Figure 2~~, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

41. (Currently Amended) The method of claim 15, wherein the ~~relative~~ structural coordinates comprise the ~~relative~~ x-ray structural coordinates of the active site of P-selectin LE

crystal according to Figure 2 ~~Figure 5~~, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

42. (Canceled)

43. (Previously Presented) The method of claim 15, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å .

44. (Previously Presented) The method of claim 15, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

45. (Previously Presented) The method of claim 66, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å.

46. (Previously Presented) The method of claim 66, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

47. (Previously Presented) The method of claim 40, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å.

48. (Previously Presented) The method of claim 40, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

49. (Previously Presented) The method of claim 41, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å.

50. (Previously Presented) The method of claim 41, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

51. (Canceled)

52. (Canceled)

53. (Currently Amended) The method of claim 15, wherein the identifying step (c) comprises determining a fit between the three-dimensional representation of the active site of P-selectin LE and a three-dimensional structure of the candidate agent. ~~wherein the three-dimensional model is generated using the relative structural coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.~~

54. (Previously Presented) The method of claim 15, wherein the three dimensional model is generated using the relative structural coordinates according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

55. (Previously Presented) The method of claim 15, wherein the three dimensional model is generated using the relative structural coordinates according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

56. (Currently Amended) A method for identifying ~~an~~ a candidate agent that interacts with P-selectin LE, comprising the steps of:

(a) providing a three-dimensional structure of ~~crystal comprising a~~ P-selectin LE, ~~wherein~~ the three-dimensional structure being obtained by subjecting a crystal comprising P-selectin LE to x-ray diffraction and collecting data sufficient to determine the three-dimensional structure of said P-selectin LE, ~~crystal has a space group $P2_1$ or I222 and the P-selectin LE~~ wherein said P-selectin LE consists of ~~comprises~~ the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:9, ~~or conservative substitutions thereof~~ and said crystal is characterized by space group $P2_1$ with unit cell parameters of a=81.0Å, b=60.8Å, c=91.4Å, and beta=103.6°; or by

space group $P2_1$ with unit cell parameters of a=81.1Å, b=60.5Å, c=91.4Å, and beta=103.3°; or by space group I222 with unit cell parameters of a=63.4Å, b=96.8Å, and c=187.3Å;

~~obtaining the relative structural coordinates of an active site of said P selectin LE crystal, wherein the relative structural coordinates comprise the relative structural coordinates of the active site of P-selectin LE crystal according to Figures 2,3 or 5 ± a root mean square deviation from the backbone atoms of said amino acids of no more than 1.5Å;~~

(b) generating a three dimensional model from said three-dimensional structure of P-selectin LE; ~~using said relative structural coordinates of the active site of the P-selectin LE crystal;~~

(c) identifying the amino acid residues forming the active site of P-selectin LE from the three-dimensional model in step (b) in order to generate a three-dimensional representation of the active site of P-selectin LE;

(d) employing said three-dimensional representation from step (c) ~~model~~ to design or select ~~an~~ the candidate agent that interacts with P-selectin LE; and

(e) contacting said candidate agent with said P-selectin LE to determine the ability of said candidate agent to interact or bind said P-selectin LE;

whereby the detection of the ability of said candidate agent to interact or bind said P-selectin LE thereby identifies said candidate agent as an agent that interacts with P-selectin LE.

~~obtaining the designed or selected agent.~~

57. (Currently Amended) The method of claim 56, further comprising ~~wherein obtaining the agent comprises synthesizing~~ contacting the candidate agent with P-selectin LE in order to determine the effect the agent has on P-selectin LE activity.

58. (Currently Amended) The method of claim 56, wherein the three dimensional structure of P-selectin LE ~~model is generated using~~ comprises the ~~relative~~ x-ray structural coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å .

59. (Currently Amended) The method of claim 56, wherein the three dimensional structure of P-selectin LE ~~model is generated using~~ comprises the ~~relative~~ x-ray structural coordinates according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å .

60. (Currently Amended) The method of claim 56, wherein the three dimensional structure of P-selectin LE ~~model is generated using~~ comprises the ~~relative~~ x-ray structural coordinates according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

61. (Currently Amended) The method of claim ~~15 or~~ 56, wherein the x-ray structural coordinates of the amino acid residues forming the active site of P-selectin LE according to step (c) are selected from the group consisting of:

(i) the x-ray structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, LYS111, and LYS113 according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

(ii) the x-ray structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYS113, and HIS114 according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

~~P-selectin LE comprises the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:9, and the crystal has space group $P2_1$ with unit cell parameters of a=81.0Å, b=60.8Å, c=91.4Å, and beta=103.6°.~~

62. (Currently Amended) The method of claim ~~15 or~~ 56, wherein the P-selectin LE in the crystal is complexed with SLe^x.

63. (Currently Amended) The method of claim 62, wherein the P-selectin LE ~~comprises~~ consists of the amino acid sequence of SEQ ID NO:6 ~~SEQ ill NO:6~~, SEQ ID NO:8 ~~SEQ 1D NO:S~~ or SEQ 1D NO:9, and the crystal has space group $P2_1$ with unit cell parameters of a=81.1Å, b=60.5Å, c=91.4Å, and beta=103.3°.

64. (Currently Amended) The method of claim ~~15 or~~ 56, wherein the P-selectin LE in the crystal is complexed with a PSGL-1 peptide.

65. (Currently Amended) The method of claim 64, wherein the P-selectin LE comprises the amino acid sequence of SEQ 1D NO:6, SEQ ID NO:8 or SEQ ID NO:9, and the crystal has space group I222 with unit cell parameters of a=63.4Å, b=96.8Å, and c=187.3Å.

66. (Currently Amended) A method for identifying an agent that interacts with P-selectin LE, comprising:

providing the x-ray ~~relative~~ structural coordinates of a P-selectin LE which comprises the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:9, ~~or conservative substitutions thereof,~~ wherein the ~~relative~~ x-ray structural coordinates of the active site of P-selectin LE are selected from the group consisting of:

(i) the ~~relative~~ x-ray structural coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å;

(ii) the ~~relative~~ x-ray structural coordinates of amino acids TYR44, SER46, SER47, TYR48, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, ARG85, GLU88, CYS90, GLU92, ILE93, TYR94, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, LYS111, and LYS113 according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å; and

(iii) the ~~relative~~ x-ray structural coordinates of amino acids SER6, THR7, LYS8, ALA9, TYR10, SER11, TYR44, TYR45, SER46, SER47, TYR48, TYR49, TRP50, ALA77, ASP78, ASN79, GLU80, PRO81, ASN82, ASN83, LYS84, ARG85, ASN86, ASN87, GLU88, CYS90, GLU92, ILE93, TYR94, ILE95, LYS96, SER97, PRO98, SER99, ALA100, TRP104, ASN105, ASP106, GLU107, HIS108, CYS109, LEU110, LYS111, LYS112, LYS113, and HIS114 according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å;

generating a three-dimensional model of P-selecting LE using said ~~relative~~ x-ray structural coordinates of the active site of P-selectin LE; and

evaluating the fit between the three dimensional model of the active site and a candidate agent; thereby identifying the agent.

67. (Currently Amended) The method of claim 66, wherein the ~~relative~~ structural coordinates of the active site comprise the coordinates according to Figure 2, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

68. (Currently Amended) The method of claim 66, wherein the ~~relative~~ structural coordinates of the active site comprise the coordinates according to Figure 3, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

69. (Currently Amended) The method of claim 66, wherein the ~~relative~~ structural coordinates of the active site comprise the coordinates according to Figure 5, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

70. (Currently Amended) The method of claim 66, further comprising detecting the ability of the candidate agent to bind in vitro or in vivo to the active site of P-selectin LE. ~~wherein the P-selectin LE comprises the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:9.~~

71. (Previously Presented) The method of claim 66, wherein the step of evaluating the fit between the three dimensional model of the active site and the candidate agent comprises performing computer fitting analysis of the agent with the three dimensional model.

72. (Currently Amended) The method of claim 66 [[56]], further comprising contacting the designed or selected agent with P-selectin LE in order to determine the effect the agent has on P-selectin LE activity.

73. (New) The method of claim 56, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å .

74. (New) The method of claim 56, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.

75. (New) The method of claim 56, further comprising detecting the ability of the candidate agent to bind in vitro or in vivo to the active site of P-selectin LE.

76. (New) The method of claim 56, further comprising synthesizing said candidate agent.

77. (New) The method of claim 66, further comprising synthesizing said candidate agent.

78. (New) The method of claim 15, further comprising detecting the ability of the candidate agent to bind in vitro or in vivo to the active site of P-selectin LE.

79. (New) The method of claim 39, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 1.0Å .

80. (New) The method of claim 39, wherein the ± a root mean square deviation from the backbone atoms of said amino acids is not more than 0.5Å.